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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/549,937	04/14/2000	Michael B Chancellor	2710-4007US2	9119

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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/549,937	CHANCELLOR ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/9/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *107-153* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *108,113-118,121-124,127-132 and 137-153* is/are rejected.

7)☒ Claim(s) *107,109-112,119,120,125,126 and 133-136* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/16/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/9/03 has been entered.

Claims 107-153 are pending.

Applicant's traversal, the cancellation of claims 1-106, the amendment to the specification, the addition of claims 107-153 in paper filed on 9/9/03 is acknowledged and considered.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 107-112 of this application.

The reasons for why claims 107-112 are not supported by the provisional 60/ 083,917 as discussed herein:

Claims 107-112: The provisional provides support under 112 first paragraph written description for isolating MDCs by re-plating non-adherent cells from step(a) in a second

collagen-coated container when approximately 15-20% of cells from the cell suspension have adhered to the first container. However, the provisional application does not provide sufficient written description for a for isolating MDCs by re-plating non-adherent cells from step(a) in a second collagen-coated container when approximately 30-40% of cells from the cell suspension have adhered to the first container.

Applicant's claim for domestic priority under 35 U.S.C. 120 is acknowledged. However, the US application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 107-112 of this application.

The reasons for why claims 107-153 are not supported by the US application 09/302,896 discussed herein:

Claims 107-112: US application '896 provides support under 112 first paragraph written description for isolating MDCs by re-plating non-adherent cells from step(a) in a second collagen-coated container when approximately 15-20% of cells from the cell suspension have adhered to the first container. However, US application '896 does not provide sufficient written description for a for isolating MDCs by re-plating non-adherent cells from step(a) in a second collagen-coated container when approximately 30-40% of cells from the cell suspension have adhered to the first container.

Drawings

The drawings were received on 7/28/03 drawings. These drawings are acceptable.

The petition for color drawings filed on 7/28/03 has been GRANTED.

Specification

The disclosure is objected to because of the following informalities: the status (e.g., pending, abandoned, patented US Patent No.) of US applications listed on page 14, line 30, page 15, lines 2 and 7, page 28, line 31, page 29, line 17 is missing.

Claim Objections

Claim 107 is objected to because of the following informalities: several periods in the claim. See MPEP 608.01(a). Claims 108-115 are objected to because they are dependent on claim 107. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 108 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 108, as best understood, is readable on a genus of an isolated mammalian muscle-derived progenitor cells (MDC), and wherein the cells express cell markers selected from the

group consisting of CD34, Bcl-2, Sca-1 and Flk-1 and do not express CD45 and c-kit cell markers, wherein the genus of MDCs is not claimed in a specific biochemical structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates a genus of isolated mammalian MDCs having a long term survivability when introduced into mammals recipient host, wherein the long-term survivability is determined by viability or proliferation of the cells as muscle tissue cells at or near a site of introduction for greater than or equal to about two weeks following subcutaneous injection into (i) a severe combined immune deficient (SCID) mouse model system or (ii) the recipient host. The claims read on isolating a genus of MDCs from any muscle tissue (e.g., skeletal, smooth). The as-filed specification provides sufficient description of a species of isolated cells (pp6) from skeletal muscle of a mouse having long-term survivability. The examples in the specification isolate cells (pp6) from skeletal muscle of mdx mice, female SD rats and SCID mice. The pp6 cells were examined by immunohistochemical analysis by the expression of cells markers (pages 29-30, Table 1). The pp6 cells displayed several markers (see Table 1), including Flk-1 a mouse homologue of human KDR gene, which was recently identified as a marker of hematopoietic cells with stem-like characteristics. Furthermore, the pp6 cells display a CD34 marker and the art of record teaches that although the reversible expression of CD34 remains to be determined in muscle derived stem cells, the use of CD34 as a marker of muscle-derived stem cells should at least by used with caution. "Stem cell antigen-1 (Sca-1) and CD34 are the markers most

frequently used to characterize the MDSC, although Sca-1 expression is the only the only marker consistently identified on the multipotent cells (Deasy et al., Current Opinion in Molecular Therapeutics, 4:382-389, 2002)." The art of record displays the variability of murine muscle-derived progenitor cells, see Qu et al., Journal of Cell Biology, Vol. 142, pp. 1257-1267, 1998 (IDS) and Lee et al., The Journal of Cellular Biology, Vol. 150, 2000, pp. 1085-1099 (IDS). The art of record further teaches that a recent report has suggested that only a discrete minority of myoblast can survive after implantation and thus may represent a population of myogenic stem cells (See Lee, *supra*).

Furthermore, the disclosure does not provide an adequate written description of a representative number of species of isolated mammalian muscle-derived progenitor cells, which functions as intended in the claimed invention. It is not apparent from the specification that the description of phenotypic markers is essential for the biological function of the muscle-derived progenitor cells having long term survivability. The structure that is required for an adequate description of a representative number of species as embraced by the claimed genus of isolated mammalian muscle-derived progenitor cells is not described sufficiently in the specification. As stated above, a mere statement asserting that any cell having the phenotypic markers without providing the essential elements does not lend evidentiary support for a skilled artisan to have recognized that the applicant was in possession of the genus of cells having a phenotype as claimed, particularly since the skill and knowledge in the art is not adequate to determine the structure of the representative number of species of mammalian muscle-derived progenitor cells that is essential for the biological function as intended by the claimed invention on the basis of

the disclosure of only one species consisting of an isolated murine muscle-derived progenitor cells.

It is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or potential markers of cells that are essential for a genus of an isolated mammalian muscle-derived progenitor cells as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of MDCs with the markers of a genus of isolated MDCs that must exhibit the disclosed biological functions as contemplated by the claims.

The contemplation in the specification for a genus of MDCs is not sufficient to support the present claimed invention directed to a genus of isolated mammalian muscle-derived progenitor cells expressing desmin as a cell surface protein. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of isolated mammalian muscle-derived progenitor cells that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would

recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of isolated mammalian muscle-derived progenitor cells that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Applicant's arguments filed 9/9/03 have been fully considered but they are not persuasive.

Applicants argue that should phenotypic marker analysis be performed on the MDCs isolated by the presently claimed method, such analysis can be used to further characterize the MDCs obtained by the claimed isolation method. It is recognized by those having skill in the relevant art that certain phenotypes markers may shared among many mammalian species, while others have species counterparts that perform similar function. See page 13 of applicants' traversal.

Applicants' argument is not found persuasive because the specification only provides sufficient description of pp6 cells from murine or rats. The specification contemplates a means to assess whether isolated MDC are viable and proliferate and survive as claimed by injecting into SCID mice and assessing whether the cells are viable for muscle tissue cells at a time of at least two weeks after injection. However, in view of the art of record and applicants' argument, the contemplation displays that applicants did not have possession of a representative number of

isolated muscle-derived progenitor cells to represent the claimed genus to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Declaration of Dr. Chancellor under 37 CFR 1.132 filed 11/21/02 is insufficient to overcome the rejection of claim 108 based upon 112 first paragraph written description as set forth in the instant Office action because: the specification only teaches how to isolate or obtain the claimed MDC from explants of mdx and SCID mice and SD female rats. "Stem cell antigen-1 (Sca-1) and CD34 are the markers most frequently used to characterize the MDSC, although Sca-1 expression is the only the only marker consistently identified on the multipotent cells (Deasy et al., Current Opinion in Molecular Therapeutics, 4:382-389, 2002, Dr. Huard is co-author of this article and Dr. Huard is an applicant in the instant application)."

With respect to the statement by Dr. Chancellor that, "Successful practice of the claimed invention is within the capability and know-how of the skilled practitioner with no requirement for undue or unreasonable experimentation," the statement is not supported by any evidence in the specification. Furthermore, the art of record teaches the limitations of stem cells in cell therapy applications, e.g., heterogeneity in phenotype, identification and isolation of stem cells (Deasy et al., *supra*).

The statement by Dr. Chancellor in the declaration that the method used for isolating mouse and rat MDCs can be used to isolate MDCs from other animals (see pages 2-3 and 8) displays that the specification was not in possession of a representative number of species of the claimed isolated mammalian muscle-derived progenitor cells to support the genus of claimed

MDCs to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Declaration of Dr. Cannon under 37 CFR 1.132 filed 7/28/03 is insufficient to overcome the rejection of claims based upon as set forth in the instant Office action because: of the reason(s) of record. Furthermore, absence evidence to the contrary, the Declaration of Dr. Cannon is directed to addressing the 112 first paragraph enablement and not addressing the 112 first written description rejection. The written description requirement is separate and distinct from the enablement requirement. See MPEP 2161.

Claims 108, 127-129, and 137-153 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated murine muscle-derived progenitor cells (MDCs), wherein the cells are pp6 and the cells express desmin and the cell markers CD34, Sca-1, Flk-1, and Bcl-2 and do not express CD45 and c-Kit; using MDCs in a method of augmenting or bulking muscle tissue in a recipient; and isolated clonal murine muscle-derived progenitor cells (mc13), wherein the clonally isolated cells express desmin and express the cell markers Flk-1, Sca-1 and do not express CD34, CD45, and c-Kit, and does not reasonably provide enablement for a genus of isolated muscle-derived progenitor cells express desmin and the cells also express a cell marker selected from the group consisting of CD34, Bcl-2. Sca-1, and Flk-1; and using the cells in a genus of therapeutic methods contemplated by the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claimed invention is directed to using MDCs to treat an injured, damaged, or dysfunctional muscle tissue (skeletal or smooth) in a recipient. The invention lies in the field of cell therapy.

The art of record for cell transplantation (e.g. myoblast) has been hindered by various limitations: immune rejection, poor cellular survival, and the limited spread of the injected cells (Lee et al., The Journal of Cellular Biology, Vol. 150, 2000, pp. 1085-1099, IDS). Lee further teaches that, "skeletal muscle tissue has been extensively investigated as a potential source for isolation of pluripotent stem cells. A recent report has suggested that only a discrete minority of myoblast can survive after implantation and thus may represent a population of myogenic stem cells. In 1998, a specific population of highly purified muscle derived cells by the pre-plate technique that significantly improved cell survival after transplantation when injected intramuscularly." Although the mechanism by which these specific muscle derived cells display a high cell survival is unclear (page 1086). "Comparison of the muscle-derived cells to other types of muscle-derived cells indicates that more studies are required to accurately assess the origin and more importantly, the functional property of these various populations of muscle-derived stem cells (page 1096-1097)."

In addition, the art of record teaches, "the study of muscle satellite cells as a stem cell and it role in skeletal muscle is still in its infancy and it will now be important to characterize the influence of growth factors and components of the extracellular matrix responsible for activating genetic responses within stem cells (Seale et al., Developmental Biology, 2000, page 122, IDS)."

Thus, at the time the application was filed, the art of record for the production or isolation of a genus of muscle-derived progenitor cells was considered unpredictable.

The specification provides working examples briefly described below:

Example 1 teaches the preparation of mouse muscle derived cells (MDC), pp6 (pages 28-30). Examples 3-5 and 7-8 display that genetically modified MDC with Lac Z were viable for up to 4 weeks in the lower abdomen of rats as shown in Example 3 (pages 32-33 and 39-40). Example 6 displays an increase in the contraction amplitude and contraction velocity of bladder strips of cryodamaged bladder tissue in rats using MDC (pages 33-39). Example 9 displays that genetically modified mc13 cells with adBMP-2 can cause bone formation (pages 40-51).

In view of the In re Wands Factors, the specification provides sufficient guidance for one skilled in the art to make murine rat pp6 cells and the clonal muscle-derived cells, mc13 from murine pp6. However, in view of the lack sufficient guidance provided by the specification for making the genus of mammalian muscle-derived cells and the art of record stating that the functional properties of the various populations of muscle-derived cells require further research (Lee, pages 1096-1097); it is not apparent if cells from a different mammal with the same phenotypic markers would exhibit the same mechanisms because of the different markers displayed by other mammals.

Furthermore, with respect to claim 108 directed to MDCs expressing specific cell markers. The claim is directed to isolating a genus of MDCs from any muscle tissue (e.g., cardiac, skeletal, smooth). The specification teaches isolating MDCs from rat and mouse skeletal muscle. The specification does not teach isolating MDCs from any other type of muscle tissue. The as-filed specification and the art of record do not teach a nexus between isolating

MDCs from skeletal muscle to isolating MDCs from any other muscle tissue. The art of record further teaches that:

> The expression of CD34 is reversible on hematopoietic stem cells. In fact, the art suggest that CD34 is probably a marker of activated stem cells, but it is not necessarily expressed in all stem cells. Although the reversible expression of CD34 remains to be determined in muscle derived stem cells, the use of CD34 as a marker of muscle-derived stem cells should at least by used with caution. Cells isolated at pp2 in our experiments are highly different than the cells isolated at pp6 in term of marker expression in vitro as well as their functional properties in vivo, see Qu and Lee.
>
> Progenitor cells give rise to related types of cells-lymphocytes, such as T cells, B cells, and natural killer cells, for example-but in their normal state do not generate a wide variety of cell type as such are not truly stem cells. It is necessary to show that the adult stem cell give rise to cell types that normally occur in different tissue. Neither of these criteria are easily met. (NIH: News: Stem Cells; Scientific Progress and Future Research Directions [online], June 2001, Executive Summary, ES-3, Appendix D, D-11 and D-12, and Chapter 4, page 23-25, 36, and 38, http:/www.nih.gov.news/stemcell/scireport.htm, retrieved online 5/15/02).

The pp6 cells displayed several markers (see Table 1), including Flk-1 a mouse homologue of human KDR gene, which was recently identified as a marker of hematopoietic cells with stem-like characteristics. Stem cell antigen-1 (Sca-1) and CD34 are the markers most frequently used to characterize the MDSC, although Sca-1 expression is the only the only marker consistently identified on the multipotent cells (Deasy et al., *supra*)." In view of the specification and the art of record it appears that the pp6 cells have different markers than other mammalian species, therefore, the pp6 cells would not be in other mammalian species. One skilled in the art would have to further experiment with different muscle types and different mammals and determine which cells meet the limitation set forth in the claim. Thus, in view of the In re Wands Factors, it would require an undue amount of experimentation for one skilled the art to reasonably extrapolate from making and using pp6 cells from a mouse or a rat to making and using a genus of muscle-derived progenitor cells.

With respect to the claimed methods (claims 127-129 and 137-153), the specification only enables one skilled to use MDCs in a method of augmenting or bulking smooth muscle tissue or skeletal muscle tissue in a recipient. It would take one skilled in the art an undue amount of experimentation to reasonably correlate from the working examples to a genus therapeutic methods in a recipient because of the lack of guidance for making a genus of isolated MDCs with the desired markers. Furthermore, the breadth of the instant invention as claimed embraces repairing injured, damaged or dysfunctional i) esophageal muscle tissue, ii) gastroesophageal, iii) sphincter muscle tissue, iv) ureteral-bladder muscle tissue, iv) heart muscle, or v) bladder tissue in a recipient by administering an undefined population of undifferentiated muscle derived progenitor cells (U-MDCs). However, the specification does not disclose a working example for each claimed method. The art of record teaches, "While much of the attention has been focused on bone and cartilage healing in orthopedic-related injuries, less emphasis has been directed to comprehending the normal and abnormal development of muscle tissue (Kasemkijwattana et al., Cell Transplantation, 7:585-598, 1998, IDS). The office conducted a prior art search of the claimed methods against prior art databases and the results from the search did not display any cell therapy to treat injured, damaged or dysfunctional esophageal muscle tissue or gastroesophageal. Each muscle tissue embraced by the claimed invention has a different structure and function and the specification lacks guidance from correlating from the working examples to treating a genus of muscle tissue injuries or disorders. The as-filed specification fails to disclose that the injection of MDCs derived from any type of muscle (skeletal or smooth) into a recipient would lead to a treatment of an injured, damaged, or dysfunctional tissue. In addition, the specification fails to disclose that MDCs would provide

immune protection to MDCs of xenogenic or allogenic origin. The art of record teaches that altering the immune system of the host could potentially affect the fusion of transplanted myoblast. Furthermore, immunosuppressive agents may be directly toxic to host muscle (Rando, IDS).

Furthermore, the specification fails to provide sufficient guidance for one skilled in the art to reasonably extrapolate from the specification to treating any muscle disorder embraced by the claimed invention. With respect to the working examples directed to treating stress urinary incontinence (SUI), the art of record teaches that SUI occurs when urethral sphincter muscle is not sufficiently strong to prevent urine leakage for example while coughing or jumping. SUI is associated most often with pelvic floor muscle laxity. Weakened and stretched out muscles and connective tissue lead to reduce muscle tensions in the sphincter complex that's insufficient to keep the urethra closed tightly when pressure increases. Furthermore, urinary incontinence is the result of mixed and urge and stress incontinence (Newman et al., Am. J. Nurs. 103:46-55, 2003). The uretheral afferent nerve activity affects the micturition reflexes, indicating that in patients with SUI, the leakage of urine proximal urethra stimulates afferent nerve, which facilitate voiding reflexes (Jung et al., The Journal of Urology, 162:204-212, 1999). Furthermore, detrusor weakness is a slowly progressing problem in human, whereas the murine model as disclosed in the instant specification has only shown physical improvement following an acute cryo-induced injury. The state of SUI art teaches that the graft success and the physiological improvement observed in the rodent-model may be absent in chronic weakness usually associated with human (Huard et al., Gene Therapy 9:1617-1626, 2002). The Gene Therapy article (where Dr. Chancellor is one of the authors) recites that the graft success and the

physiological improvement observed in the murine-model may be absent in chronic weakness usually associated with stress urinary incontinence in humans (supra). Furthermore, Lee et al., (Int. Urogynecol J, 14:31-37, 2003, where Dr. Huard and Dr. Chancellor are co-authors) teach, "There are limitations to this animal model in that rats are quadrupeds and do not normally exert the same forces on their pelvis as do human females."

Furthermore, the as-filed specification fails to provide teaching what would be the appropriate dose of muscle-derived cells per route of administration for a sustained and high enough level of expression of transplanted cells to treat each disorder embraced by the claimed methods.

The art of record displays the unpredictability of muscle-derived cells differentiating into a specific muscle tissue. Kasemkijwattana et al. (Cell Transplantation, 1998, IDS) discloses that although muscle injury is capable of healing, an incomplete functional recovery often occurs (abstract) and the best treatment for muscle injury has not yet been defined and the recommended treatment regimens for contusions have varied widely, depending on the severity of the injury (page 585).

Furthermore, Ledley, *Pharmaceutical Research*, Vol. 13, pp. 1595-1614, 1996 (cited on a previous PTO-892), discloses that "while transplantation of hepatocytes, pancreatic cells, myoblasts, epidermal cells, neuronal cells, synovial cells, and fibroblasts has been demonstrated in animals, these methods are not routinely available for treating any medical disease or disorder in any animal including humans (page 1596)."

In the absence of essential teachings specific to the making and using a genus of isolated muscle-derived progenitor cells, it would require an undue amount of experimentation for one

skilled in the art to reasonably extrapolate from the specification to practicing the full scope of the claimed invention.

Therefore, considering the unpredictability in the state of SUI art and limited amount of guidance provided by the instant specification, it is highly unpredictable that the administration of MDCs (autologous or allogenic) would ameliorate injured, damaged or dysfunctional i) esophageal muscle tissue, ii) gastroesophageal, iii) sphincter muscle tissue, iv) ureteral-bladder muscle tissue, iv) heart muscle, or v) bladder tissue in a recipient.

In conclusion, the as-filed specification and claims coupled with the art of record at the time the invention was made only provide sufficient guidance and/or evidence to reasonably enable for isolated murine muscle-derived progenitor cells, wherein the cells are pp6 and express desmin and express cell markers CD34, Sca-1, Flk-1, and Bcl-2 and do not express CD45 and c-Kit and using MDCs in a method of augmenting or bulking muscle tissue in a recipient. One skilled in the art would have to engage in a large quantity of experimentation in order to practice the full scope of the claimed invention based on the application's disclosure, the unpredictability of making and using mammalian muscle-derived progenitor cells with any phenotype (e.g., cell markers) selected from the group consisting of desmin, CD34, Bcl-2 and Sca-1 or Flk-1, and the problems in the art of record for using MDCs for treating a muscle disorder in a recipient.

Applicant's arguments filed 9/9/03 have been fully considered but they are not persuasive. The as-filed specification only teaches how to make murine and rat pp6 cells and the breadth of the claims encompass making and using a genus of mammalian isolated muscle-derived progenitor cells. One cell marker (Flk-1) found on pp6 murine cells is not found on other types of mammalian cells and the art of record displays concern with using the CD34

marker as a cell marker. The as-filed specification does not provide sufficient guidance or factual evidence for one skilled in the art to reasonably extrapolate from murine or rat pp6 cells to a genus of isolated muscle-derived progenitor cells and express cell markers selected from the group consisting of desmin, CD34, Sca-1, Flk-1, and Bcl-2 and do not express CD45 and c-Kit. Furthermore, the art of record teaches the unpredictability of isolating a genus of mammalian muscle-derived progenitor cells embraced by the claimed invention. The specification does not teach one skilled in the art what cells would or would not be operable in the claimed invention without further experimentation. Thus, in view of the In Re Wands Factors, the as-filed specification does not provide sufficient guidance or factual evidence for one skilled in the art to make and use a genus of isolated muscle-derived progenitor cells.

With respect to applicants' argument that applicants have previously presented publications of the inventors' work own work, in collaboration with their technical laboratory researchers, which are cumulative to the instant disclosure and support long-term survival of MDCs and resulting myofibers formation and bladder wall. However, it is the specification at the time of filing, not art (post-filing articles, published 2-3 years after the application's filing date) that must enable the claimed invention. The as-filed specification does not provide sufficient guidance and/or factual evidence for how to overcome unpredictability of making and using a genus of isolated muscle-derived progenitor cells.

In addition, the court in Enzo 188 F.3d at 1374, 52 USPQ2d at 1138 states:

> It is well settled that patent applications are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed.
> In re Vaeck, 947 F.2d 48, 496 & n.23. 30 USPQ2d 1438, 1445 &n23 (Fed. Cir. 1991)(citation omitted). Here, however, the teachings set forth in the specification provide no more than a

"plan" or "invitation" for those of skill in the art to experiment...; they do not provide sufficient guidance or specificity as to how to execute that plan. See Fiers v. Revel. 984 F.2d.1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993); In re Wright, 999 F.2d...[1557], 1562, 27 USPQ2d...[1510], 1514. [footnote omitted].

On this record, it is apparent that the specification provides no more than a plan or invitation in view of the art of record exemplifying the unpredictability of using any muscle derived progenitor cell in the claimed methods, for those skilled in the art to further experiment with progenitor cells so as to provide isolated muscle-derived progenitor cells as intended by the as-filed specification at the time the invention was made.

See also Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997)

> ("Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the public to understand and carry out the invention.")

In view of the art of record and the lack of guidance provided by the specification; the specification does not provide reasonable detail for what protocols are required for a genus of isolated muscle-derived progenitor cells other than pp6 from rat and mice, and it would take one skilled in the art an undue amount of experimentation to reasonably extrapolate from the scope listed above to the full scope of claimed invention.

The applicants argue that the presently claimed invention sufficiently and effectively supports the repair of injured, damaged, or dysfunctional sphincter, bladder, or urethral muscle of the genitourinary tract following introduction of MDC into the relevant tissue. The applicants argue that experimental work based on the instant application further demonstrates that MDC isolated from both mice and rats can be used as described in the specification. Applicants argue

that the cryo-induced injury to the urethra in rodents is an art recognized and accepted animal model system to test and evaluate treatments and therapies for genitourinary tract disorders and dysfunctions. Applicants argue that assessment of leak point pressure (LPP) art recognized parameter to assess MDC efficacy in the restoration of function and repair of urethral tissue. Increased LPP equates with increased continence and is an accepted parameter for assessing continence in clinical cases as well as in animal models of SUI. Accordingly the applicants concluded that experiments conducted in the cited references after the filing of the instant application, shows the beneficial effects of MDC for treating incontinence. However, this is found not fully persuasive because the evidence provided in the declaration is only limited to the amelioration of cryo-induced injury to the urethra muscles in rodents, whereas the scope of invention as claimed encompasses repair and ameliorate of an injury, damage or any dysfunction (motor or neurological) of urethra muscle tissue, sphincter muscle tissue, genitourinary tract tissue, cardiac tissue, or bladder tissue. Furthermore, applicants argument that the administration of MDC would restores the function of injured, damaged or dysfunctional uro-genital tissues (as claimed) has been found not persuasive because scope of invention as claimed is not limited to engraftment of MDC but encompasses undifferentiated muscle derived cells. In contradiction to applicants' assertions, the article published in the journal Gene Therapy 9:1617.25. 2002, (where Dr. Chancellor is one of the author) states that the graft success and the physiological improvement observed in the murine-model may be absent in chronic weakness usually associated with stress urinary incontinence in humans (supra). Furthermore, Lee et al., (Int. Urogynecol J, 14:31-37, 2003, where Dr. Chancellor is an author) teach, "There are limitations to this animal model in that rats are quadrupeds and do not normally exert the same forces on

their pelvis as do human females." At best the instant specification teaches the injection of myoblast cell line (not MDC as claimed) expressing beta-galactosidase into the urethral wall of adult female rat with cryo-induced uretheral injury. The instant specification fails to provide any evidence that administration of an undefined population undifferentiated muscle-derived cells would treat stress urinary incontinence by repairing injured, damaged or dysfunctional urethra muscle tissue, ii) sphincter muscle tissue iii) genitourinary tract tissue or iv) cardiac tissue, or v) bladder tissues. The specification fails to define what constitutes a population of undifferentiated muscle-derived cells. It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (19663, Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

In the instant case treatment of stress urinary incontinence by administering an undefined population of undifferentiated muscle-derived cells is not considered routine in the art and without sufficient guidance to a specific undifferentiated MDC cell type, and etiology of urinary incontinence in a particular type SUI, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731 , 8 USPA2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of

claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

With respect to applicants argument that, "a mechanism need not be known or understood in order for an invention to be patentable," the argument is not found persuasive because the specification fails to provide sufficient guidance and/or factual evidence to practice the broad scope of the claimed method. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991) and Enzo 188 F.3d at 1374, 52 USPQ2d at 1138. The art of record, at the time the application was filed (5/1/98), teaches the unpredictability of making a genus of isolated muscle derived progenitor cells. In view of applicants' argument, one skilled in the art would have to further experiment on cells isolated from muscle tissue and determine which cells without guidance from the as-filed specification are considered inoperable/operable.

With respect to applicants' argument that pages 1096-107 of the Lee et al., publication, do not specifically address any limitations that would affect applicant's presently claimed invention, since applicants teach in their specification that the MDCs having pluripotency for use the claimed methods are isolated from the later platings of applicants' claimed MDC isolation method, the argument is not found persuasive. The argument is not found persuasive because the claimed invention embraces a broad group of MDCs. The art of record teaches that unpredictability of making a genus of isolated MDCs. Richler et al., use a similar pre-plating method to applicants' preplating method and observed that cell lines different from each other in the frequency of formation of multinucleated fibers as well as in several morphological characteristics (Developmental Biology 23:1-22, 1970, cited on a PTO-1449). Richler further

teaches, "Many experimental variables as well as uncontrolled factors greatly influence the behavior of cell lines (pages 18-19)."

Applicants argue again that post-filing abstracts (4 years after the priority date of application), Exhibit 13 and Exhibit 14, support the teaching of applicant's disclosure. With respect to the MDCs displaying long-term survival, the argument is moot because the term "long term survival" is no longer recited in the claims because applicants canceled those claims without prejudice to obviate the specific rejection in the office action mailed on 3/11/03. The argument is further not found persuasive because the specification does not teach one skilled in the art in the art how to practice the genus of claimed methods and both abstracts indicate that further experiments will be performed to study the therapeutic effect of the cell transplantation. In addition, the specification does not teach how dystrophin delivery via cell transplantation and long-term survival of MDCs reasonably extrapolate to practicing the genus of claimed methods, e.g., treating a muscle disorder or injury in esophageal muscle tissue, gastroesophageal muscle tissue, sphincter muscle tissue, or bladder muscle tissue.

Furthermore, with respect to applicants' argument that post-filing abstract, Exhibit 15, supports both the actual practice of the presently claimed invention and the benefits afforded by the disclosed MDC-based treatments and therapies, the argument is not found persuasive. The abstract indicates the plasticity of a MDCs clone, mc13 and ex vivo gene therapy resulted in limited dissemination and restoration of dystrophin in the gastrocnemius muscles of lethally irradiated adult mdx mice. The claim invention is directed to cell therapy and not ex vivo gene therapy. The specification does not teach one skilled in the art how to reasonably extrapolate from the results in the post-filing abstract to practicing the claimed invention as broadly claimed.

The Declaration of Dr. Michael Chancellor under 37 CFR 1.132 filed 11/21/02 is insufficient to overcome the rejection of claims 107-153 based upon 112 first paragraph enablement as set forth in the instant Office action because: of the reasons of record. The Declaration of Dr. Chancellor was already addressed in the office action mailed on 3/11/03.

The Declaration of Dr. Cannon under 37 CFR 1.132 filed 7/28/03 is insufficient to overcome the rejection of claims based upon as set forth in the instant Office action because: in view of the In Re Wands Factors, the as-filed specification did not enable one skilled in the art to practice the full scope of the claimed invention.

With respect to the argument that obtaining a muscle cell suspension from an appropriate muscle tissue source does not require excessive experimentation, the argument is not found persuasive because the specification must be enabling as of the filing date. See MPEP 2164.05(a). The articles cited by Dr. Cannon are directed to using rat MDCs and does not teach one skilled in the art, at the time the application was filed, that obtaining a genus of MDCs with the desired cell markers in claim 108 was considered predictable. The specification does not teach one skilled in the art that there is nexus between isolating rat and mouse MDCs with the markers listed in claim 108 to a genus of MDCs with any marker listed in claim 108. The art of record teaches, "Stem cell antigen-1 (Sca-1) and CD34 are the markers most frequently used to characterize the MDSC, although Sca-1 expression is the only the only marker consistently identified on the multipotent cells (Deasy et al., Current Opinion in Molecular Therapeutics, 4:382-389, 2002, Dr. Huard is co-author of this article and Dr. Chancellor and Dr. Huard are

applicants in the instant application). In addition, Richler et al., use a similar pre-plating method to applicants' preplating method and observed that cell lines different from each other in the frequency of formation of multinucleated fibers as well as in several morphological characteristics (Developmental Biology 23:1-22, 1970, cited on a PTO-1449). Richler further teaches, "Many experimental variables as well as uncontrolled factors greatly influence the behavior of cell lines (pages 18-19)." Given the above analysis of the factors, it is concluded that the skilled artisan, at the time the application was filed, would have to conduct an excessive amount of experimentation in order to practice the claimed invention.

With respect to the argument that, "The results obtained using mouse MDC and rat models are suitable and accepted as being predictive of the results would be expected to be seen in similarly-treated human subjects. The use of animal models as reasonable predictors of treatment outcome in humans is known and accepted in the art." The argument is not found persuasive because in view of the In Re Wands Factors, the as-filed specification does not teach one skilled in the art how to practice the full scope of the claimed invention. The evidence of record does not support the statements' by Dr. Cannon. Furthermore, an article published in the journal Gene Therapy 9:1617-26. 2002, (where Dr. Chancellor and Dr. Huard are authors) states that, "the graft success and the physiological improvement observed in the murine-model may be absent in chronic weakness usually associated with stress urinary incontinence in humans (supra)." Furthermore, Lee et al., (Int. Urogynecol J, 14:31-37, 2003, where Dr. Chancellor and Dr. Cannon are authors) teach, "There are limitations to this animal model in that rats are quadrupeds and do not normally exert the same forces on their pelvis as do human females." The specification does not address these problems set forth by applicants. Given the above

analysis of the factors, it is concluded that the skilled artisan, at the time the application was filed, would have to conduct an excessive amount of experimentation in order to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 128 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 128 recites the limitation "a condition of the lumen" in line 2. There is insufficient antecedent basis for this limitation in the claim. There is more than one lumen in the body of a recipient. The metes and bounds of the limitation are not defined by the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 113 remains rejected under 35 U.S.C. 102(e) as being anticipated by Anderson et al. (US Patent No. 6,001,654, cited on a previous PTO-892). Anderson teaches isolated smooth muscle progenitor cells (column 13, lines 23-26 and column 16, lines 53-67).

Applicant's arguments filed 9/9/03 have been fully considered but they are not persuasive. Applicants argue that Anderson does not teach each every limitation of the claimed invention. The MDCs as newly described by the applicants are obtained by a plating method that is neither taught nor contemplated by the '654 patent.

Applicants argument is not found persuasive because the patentability of a product does not depend on its method of production. "If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)." See MPEP 2113. This is the case here.

The evidence of record does not support the assertion by applicants that the MDCs are not taught by Anderson. See MPEP § 716.01(c).

Claim 113 is rejected under 35 U.S.C. 102(b) as being anticipated by Huard et al. (IDS, Muscle & Nerve, pages 224-234, 1994) as evident by Rando et al., (The Journal of Cell Biology, 125:1275-1287, 1994, IDS). Huard teaches human myoblasts obtained from a postmortem biopsy of a 13 month-old boy (page 225).

The method of isolating MDCs in the instant specification (page 28) is based on the method in parent application 09/302,896. The method in application '896 is based on Qu et al. JBC, 142:1257-1267 and Rando et al., The Journal of Cell Biology, 125:1275-1287, 1994.

Rando teaches obtaining a pure population of myoblasts from primary cultures of mouse skeletal muscle, which were mixtures of myoblasts and fibroblasts using a preplating method (page 1278).

Thus, Huard anticipates the isolated MDCs in claim 113 because the MDCs obtained by the method in claim 107 contain myoblasts.

Applicant's arguments filed 9/9/03 have been fully considered but they are not persuasive. Applicants argue that Anderson does not teach each every limitation of the claimed invention. The publication does not teach or suggest applicants' claimed MDCs, which are obtained by a method that is not taught or disclosed in the 1194 Huard publication.

Applicants argument is not found persuasive because the patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)." See MPEP 2113.

The evidence of record does not support the assertion by applicants that the MDCs are not taught by Anderson. See MPEP § 716.01(c).

Claims 113, 114, and 115 are rejected under 35 U.S.C. 102(b) as being anticipated by Rando et al., (The Journal of Cell Biology, 125:1275-1287, 1994, IDS). Rando teaches isolating myoblast cells using preplating (page 1277). Rando teaches making clones from the primary myoblasts and differentiation medium (page 1277).

The method of isolating MDCs in the instant specification (page 28) is based on the method in parent application 09/302,896. The method in application '896 is based on Qu et al. JBC, 142:1257-1267 and Rando et al., The Journal of Cell Biology, 125:1275-1287, 1994. Rando teaches obtaining a pure population of myoblasts from primary cultures of mouse skeletal muscle, which were mixtures of myoblasts and fibroblasts using a preplating method (page 1278).

Thus, Rando anticipates the isolated MDCs in claim 113 because the MDCs obtained by the method in claim 107 contain myoblasts.

Claims 113, 114, 115, 130, and 131 are rejected under 35 U.S.C. 102(a) as being anticipated by Arcila et al., (J. Neurobiol 33:185-198, 1997). Aricla teaches myoblast transfer into mouse EDL muscles (page 185). The results indicate significant improvement in muscle weight (page 193). Aricla teaches myoblast used for myoblast transfer were derived from a myoblast cell line (page 186). Aricla teaches after 8 weeks of culturing a clone was identified. (pages 186-187).

The method of isolating MDCs in the instant specification (page 28) is based on the method in parent application 09/302,896. The method in application '896 is based on Qu et al. JBC, 142:1257-1267 and Rando et al., The Journal of Cell Biology, 125:1275-1287, 1994. Rando teaches obtaining a pure population of myoblasts from primary cultures of mouse skeletal muscle, which were mixtures of myoblasts and fibroblasts using a preplating method (page 1278).

Thus, Arcila anticipates the isolated MDCs in claim 113 because the MDCs obtained by the method in claim 107 contain myoblasts.

Claims 113, 114, 115, 130, 131, 132, 147, 148, and 149 are rejected under 35 U.S.C. 102(b) as being anticipated Law et al., (US 5,130,141, IDS). Law teaches a method of treating muscle weakness in a skeletal muscle of a host using a composition comprising myogenic cells (abstract and column 5). The myogenic cells include myoblast, myotube cells, and young muscle fiber cells (columns 2 and 3). Law teaches that myogenic cells may be produced by cloning methods (column 4). Law teaches injecting the cells into the host (columns 5 and 6). Law teaches a pharmaceutical formulation comprising the cells and a pharmaceutically acceptable carrier (column 7).

The method of isolating MDCs in the instant specification (page 28) is based on the method in parent application 09/302,896. The method in application '896 is based on Qu et al. JBC, 142:1257-1267 and Rando et al., The Journal of Cell Biology, 125:1275-1287, 1994. Rando teaches obtaining a pure population of myoblasts from primary cultures of mouse skeletal muscle, which were mixtures of myoblasts and fibroblasts using a preplating method (page 1278).

Thus, Law anticipates the isolated MDCs in claim 113 because the MDCs obtained by the method in claim 107 contain myoblasts.

Double Patenting

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper time-wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 116, 117, 118, 121, 122, 123, 124, 130, 137, 144, and 145 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 196, 199, 212, 215, and 244 of co-pending Application No. 09/302,896. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of co-pending application '896 are drawn to a method of treating a muscle tissue using MDCs.

In addition, they are not patentably distinct from each other because each invention encompasses the same material and methods. Therefore, the claims of the instant application and co-pending application '896 are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed 9/9/03 have been fully considered but they are not persuasive because the applicants have not provided sufficient evidence to overcome the provisional double patenting rejection.

Response to Arguments

Applicant's arguments, filed 9/9/03, with respect to 112 first paragraph written description rejection have been fully considered and are persuasive. The rejection of claims 1, 3, 17-26, 45-54, 84, 92-93, 96, 100-106 has been withdrawn because of the cancellation of the claims. However, upon further consideration, a new ground(s) of rejection is made in view of the addition of the new claims.

Applicant's arguments, filed 9/9/03, with respect to 112 first paragraph enablement rejection have been fully considered and are persuasive. The rejection of claims 1, 3, 17-26, 45-54, 84, 92-93, 96, 100-106 has been withdrawn because of the cancellation of the claims. However, upon further consideration, a new ground(s) of rejection is made in view of the addition of the new claims.

Applicant's arguments, filed 9/9/03, with respect to prior art rejection over Anderson have been fully considered and are persuasive. The rejection of claim 106 has been withdrawn because of the cancellation of the claims. However, upon further consideration, a new ground(s) of rejection is made in view of the addition of the new claims.

Applicant's arguments, filed 9/9/03, with respect to prior art rejection over Huard have been fully considered and are persuasive. The rejection of claim 106 has been withdrawn because of the cancellation of the claims. However, upon further consideration, a new ground(s) of rejection is made in view of the addition of the new claims.

Applicant's arguments, filed 9/9/03, with respect to double patenting rejection over co-pending application 09/302,896 have been fully considered and are persuasive. The rejection of claims 1, 3, 84, 100, 101, and 106 has been withdrawn because of the cancellation of the claims.

However, upon further consideration, a new ground(s) of rejection is made in view of the addition of the new claims.

Conclusion

Claims 107 and 109-112 are in condition for allowance because the claims are free of the prior art of record.

Claims 119, 120, 125, 126, and 133-136 are free of the prior art of record.

Claims 119, 120, 125, 126, and 133-136 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Richler et al., The Journal of Cell Biology, 125:1275-1287, 1970 and Rando et al., Journal of Cell Biology, 125: 1275-1287, teach a pre-plating method of isolating myoblast that is similar to the method in claims 107 and 109, however, neither Richler nor Rando specifically teach the limitation "when approximately 30-40% of the cells from the cell suspension have adhered to the first container" in step b) of claim 107.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER